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EXAMINER

GROSS, CHRISTOPHER M

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 12/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/540,443

Applicant(s)

POLT ET AL.

Examiner

Christopher M. Gross

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 17 April 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 9/26/2005
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

Responsive to communications entered 4/17/2006. Claims 1-10 are pending. Claims 1-10 are examined herein.

Priority

This application is a 371 of PCT/US04/05340 02/24/2004 which claims benefit of 60/449,989 02/25/2003.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed provisional application, Application No. 60/449,989, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

Specifically, provisional application 60/449,989 discloses only one disaccharide species (i.e. YtGFLS(beta-maltose)) as opposed to the breadth of the instant set of claims.

Additionally absent from provisional application 60/449,989 are packages of injectable

pharmaceuticals as set forth in claims 9 and 10. Therefore 2/24/2004 is the date for the purposes of prior art concerning claims 1-10.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3,5-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 recites vague and indefinite language in the molecule designated "MMP2005" in table 2. Table 2 does not include MMP2005, making the metes and bounds of the claimed structure unascertainable.

Claim 5 indicates the discaccharide is located on the address region of the peptide, however the disclosure does not succinctly point out the metes and bounds of the "address region" In particular, paragraph 00017 states "the address portion appears to control membrane binding and may serve to help modify receptor specificity" but does not provide any structural limitation(s). Therefore, claim 5 and all dependent claims are rejected under 35 USC 112, second paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Hovart et al (1986 Synthesis 3:209-211 – IDS entry 9/26/2005) and evidenced by Egelton et al (2001 J. Pharmacology and Experimental Therapeutics 299:967-972 – IDS entry 9/26/2005)

The claimed invention is drawn to a method for modifying a peptide enkephalin to enable the molecule to be transported across the blood-brain barrier, the method comprising the step of adding to the peptide a disaccharide moiety.

Claims 5-7 represent variations thereof.

Hovart et al teach, throughout the document, and especially in compounds 8a-f, a method of preparing enkephalin disaccharide pseudoureas.

Egelton et al teach glycosylation improves blood-brain barrier (BBB) penetration, thus said property of crossing the BBB, set forth in claim 4 is inherent in the glycosylated enkephalin peptides such as those of Hovart et al.

Hovart teach linking the peptide YGGFL through a pseudourea linkage, which comprises an oxygen atom, therein reading on claims 5 and 6. The Carboxy group of Leucine according to Hovart et al is taken as part of the address region set forth in claim 5.

The preamble of claim 7 states, "a drug delivery package labeled for use as a human drug" Generally, no patentable weight is accorded to the preamble where it

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merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Therefore said enkephalin disaccharide pseudoureas of Hovart et al read on the glycosylated enkephalin peptide of claim 7.

Claims 1, 4-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Mitchell et al (2001 JOC 66:2327-2342– IDS entry 9/26/2005)

Mitchell et al teach, throughout the document and especially the abstract and scheme 7 the preparation of O-linked enkephalin glycopeptide analogs comprising the amino acid sequence YcGF, which reads on claims 5 and 6.

On page 2328, second paragraph, Mitchell et al teach glycosylation improves blood-brain barrier (BBB) penetration, eliciting profound analgesia in mice, therein reading on “administering to the bloodstream an effective amount” per claim 1. The said property of crossing the BBB, set forth in claim 4 is inherent in the O-linked glycosylated enkephalin peptides disclosed by Mitchell et al.

The preamble of claim 7 states, “a drug delivery package labeled for use as a human drug” Generally, no patentable weight is accorded to the preamble where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535

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F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Therefore said O linked enkephalin disaccharides of Mitchell et al read on the glycosylated enkephalin peptide of claim 7.

Claims 1,4-5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Elmagbari et al (2001 FASEB Journal 15: p A915 Abstract – IDS entry 9/26/2005).

Claim 1 is drawn to a method for delivering analgesia to an individual comprising administering to the bloodstream of the individual an effective amount of an analgesic molecule which is a glycosylated enkephalin, the glycosylation being a disaccharide sugar moiety.

Elmagbari et al teach antinociceptive potency (a measure of analgesia per figure 1 of the instant specification) is enhanced when enkephalin peptides are O-linked with beta-lactose (a disaccharide). Elmagbari et al teach said enkephalin peptides were injected in to mice, reading on “administering to the bloodstream of the individual an effective amount of an analgesic molecule” as set forth in claim 1.

The O-linked beta-lactose enkaphalins of Elmagbari et al read on the “glycosylated enkephalin” of claim 1 as well as the O-linkage limitation set forth as claim 5.

Elmagbari et al teach the disaccaride as providing an optimal balance between transport across the BBB and binding affinity, as set forth in claim 4.

The preamble of claim 7 states, “a drug delivery package labeled for use as a human drug” Generally, no patentable weight is accorded to the preamble where it

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merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Therefore said O-linked enkephalin disaccharides of Elmagbari et al read on the glycosylated enkephalin peptide of claim 7.

Claims 1-2,4-7 and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by Palian (2003 JACS 125:5823-5831– IDS entry 9/26/2005).

Palian et al teach, throughout the document and especially the abstract and scheme 1 a method for preparing enkaphalin analogs comprising the amino acid sequence YtGFLS-amide O-linked to beta maltose, which reads on the YtGF motif of claim 2 as well as the YxGF message of claim 6 and the O-linkage of claim 5.

Palian et al teach on page 5824, second paragraph glycosylation improves blood-brain barrier (BBB) penetration to produce potent analgesia in mice, therein reading on “administering to the bloodstream an effective amount” per claim 1. The said property of crossing the BBB set forth in claim 4 is inherent in the O-linked glycosylated enkephalin peptide such as that presented by Palian et al.

The preamble of claim 7 states, “a drug delivery package labeled for use as a human drug” Generally, no patentable weight is accorded to the preamble where it merely recites the purpose of a process or the intended use of a structure, and where

the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Therefore said O-linked enkephalin disaccharides of Elmagbari et al read on the glycosylated enkephalin peptide of claim 7.

Absent evidence to the contrary, packaging for use as an injectable pharmaceutical will not result in a structural difference between the YtGFLS(beta-maltose)-amide of claim 10 and the identical structure disclosed by Palian et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of **Roques et al** (US Patent 4,407,794 – IDS entry 9/26/2005) in view of **Mitchell et al** (2001 JOC 66:2327-2342– IDS entry 9/26/2005).

Roques et al teach, throughout the document and especially the abstract, enkephalin peptides including the amino acid motif YtGF set forth in claims 2-3, 6, 8-9.

Roques et al do not teach O-linked disaccharide enkephalin derivatives, however.

Mitchell et al is relied on as above. In particular, Mitchell et al teach methods of preparing enkephalin derivatives bearing lactose, cellobiose and melibiose O-linked through a C terminal serine amide residue.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to incorporate lactose, cellobiose and melibiose O-linked through a C terminal serine amide residue per Mitchell et al to YtGF motif of Roques et al.

One of ordinary skill in the art would have been motivated to add the lactose, cellobiose and melibiose O-linked through a C terminal serine amide residue per Mitchell et al to YtGF motif of Roques et al. because the glycosylation provides a means of penetrating the BBB, resulting in prolonged analgesia, as noted by Mitchell et al on page 2328, second paragraph.

One of ordinary skill could do so with a reasonable expectation of success since Mitchell et al provide extensive synthetic protocols.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Gross whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JON EPPERSON, PH.D.
PATENT EXAMINER

Christopher M Gross
Examiner
Art Unit 1639

cg

A handwritten signature in black ink, appearing to be 'C. M. Gross', written over a horizontal line.